

### **REMARKS**

This application is directed to a method of enhancing expression of a desired protein at mucosal effector sites, comprising placing the protein to be expressed under the control of a promoter and causing expression in mucosal cells. Constructs used in the methods, as well as suitable recombinant gut-colonizing microorganisms such as *Salmonella spp.* are described. Such organisms are useful in the preparation of vaccines.

Following entry of this amendment Claims 1-4, 7-15, 17-32 will be pending. Claims 1, 2, 7, 10, 11, 12, 15, 17, 19, 20, 21 and 22 are amended, and Claims 5-6, and 16 are cancelled without prejudice. Claims 23-32 are new. No new matter is added and support for the amendments is found throughout the specification.

#### ***Informalities-Specification***

In the Office Action mailed March 23, 2005 the Examiner objected to page 12 of the instant specification for referring to Figures 3a and 3b and Figures 7a and 7b as “Figure 3” and “Figure 7”. Applicants have amended the specification to recite “Figure 3a and 3b” and “Figure 7a and 7b” in lines 16 and 33 respectively.

As stated by the Examiner the use of trademark names is permissible. Applicant’s have amended the specification as necessary to capitalize such entries or provide generic terminology.

Applicants respectfully submit new headings are provided herein to place the application in better formal style for Examination. Accordingly, Applicants respectfully request withdrawal of the Examiner’s objection thereof.

#### ***Claim rejections under 35 U.S.C. § 112, first paragraph***

In the March 23, 2005 Office Action, the Examiner rejected Claims 1, 2, 11, 15, 22 and those dependents therefrom under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement.

The Examiner stated that Claims 1, 2, 11, 15, 22 recite the limitation ‘fragment’ or ‘variant’. The Examiner concluded that there is inadequate support to meet the written description requirement of the claimed invention.

Applicants respectfully submit that amendments to claims as provided herein, obviate the Examiner’s rejection. In particular, Claims 1, 2, 11 and 22 no longer recite the terms “fragment” or “variant” and thus overcome the written description requirement rejection. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

***Claim rejections under 35 U.S.C. § 112, first paragraph***

In the March 23, 2005 Office Action, the Examiner rejected Claims 1, 2, 11, 15, 22 and those dependent therefrom under 35 U.S.C. §112, first paragraph, as lacking scope of enablement. Applicants respectfully submit that the amendments to the claims overcome the rejection.

In particular, Claims 1, 2, 11 and 22 no longer recite the terms “fragment” or “variant” and thus overcome the scope of enablement rejection. As concluded by the Examiner the specification is enabled for a recombinant construct and a recombinant *Salmonella* comprising the construct wherein the construct comprises P<sub>phoP</sub> promoter having the nucleotide sequence of SEQ ID NO: 2, operatively interconnected with an isolated nucleic acid that encodes F1 antigen of *Yersinia pestis*, wherein the recombinant *Salmonella* comprising the construct induces an IgA response in a mammal to which it is administered, and a method of expressing the F1 antigen of *Yersinia pestis* using the construct in *Salmonella*. Accordingly, Applicants respectfully request withdrawal of the Examiner’s rejection under 35 U.S.C. §112, first paragraph.

***Claim rejections under 35 U.S.C. § 112, second paragraph***

In the March 23, 2005 Office Action, the Examiner rejected Claims 1-4, 7-15 and 17-22 under 35 U.S.C. §112, second paragraph, for failing to point out and distinctly claim the subject matter.

Applicants respectfully submit that the amendments to the claims as provided herein overcome rejections (a)-(q) as raised by the Examiner. Accordingly, Applicants respectfully request withdrawal of the Examiner's rejection under 35 U.S.C. §112, second paragraph.

***Claim rejections under 35 U.S.C. § 102***

In the Office Action mailed March 23, 2005, the Examiner rejected Claims 2-4, 7-15, 17-19, 21 and 22 as anticipated by Titball *et al.*, U.S. 5,985,285 (hereinafter "Titball *et al.* patent") under 35 U.S.C. §102(b). The Examiner stated that Titball *et al.* teach a live oral vaccine comprising a pharmaceutically acceptable carrier or an adjuvant and a human or animal gut colonizing microorganism that is transformed with a recombinant DNA construct expressing the heterologous F1 antigen of *Yersinia pestis* under the control of a P<sub>phoP</sub> *in vivo* inducible promoter, wherein the DNA is positioned in frame with the promoter. Applicants respectfully traverse the rejection.

Applicants respectfully submit that while Titball *et al.* discloses a range of promoters, Applicants respectfully assert that the Titball *et al.* patent fails to disclose P<sub>phoP</sub> as a promoter in an expression construct. The only promoter exemplified in the Titball *et al.* patent is the *lac* promoter. Additionally, column 3, lines 46-48 also state that the *lac* promoter and the *nirB* promoter are preferred. Accordingly, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. §102(b).

In the Office Action mailed March 23, 2005, the Examiner rejected Claims 2-4, 7-15, 17-19, 21 and 22 as anticipated by Titball *et al.*, (WO 96/28551) (hereinafter "Titball *et al.* PCT") under 35 U.S.C. §102(b). The Examiner stated that the Titball *et al.* PCT teaches a live oral vaccine comprising a pharmaceutically acceptable carrier or an adjuvant and a human or

animal gut colonizing microorganism that is transformed with a recombinant DNA construct expressing the heterologous F1 antigen of *Yersinia pestis* under the control of P<sub>phoP</sub> *in vivo* inducible promoter, wherein the DNA is positioned in frame with the promoter. Applicants respectfully traverse the rejection.

While Applicants agree that the Titball *et al.* PCT discloses a range of promoters, Applicants respectfully assert that the Titball *et al.* PCT fails to disclose P<sub>phoP</sub> as a promoter in an expression construct. Applicants respectfully submit that neither the Titball *et al.* PCT nor the Titball *et al.* patent disclose constructs that utilize the P<sub>phoP</sub> promoter as claimed herein. As a result, there is no teaching to one of ordinary skill in the art to select the P<sub>phoP</sub> promoter for use in constructs of the type disclosed herein. It is to the Applicants credit that they have observed that constructs utilizing the P<sub>phoP</sub> promoter have an unexpected advantage in terms of the expression in mucosal effector cells. For at least the above reasons, Applicants respectfully submit the subject matter of Claims of 2-4, 7-15, 17-19, 21 and 22 is novel over Titball *et al.* Accordingly, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. §102(b).

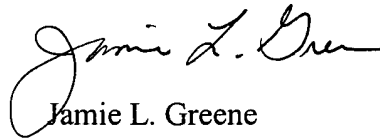
### CONCLUSION

The foregoing is submitted as a full and complete Response to the Non-Final Office Action mailed on March 23, 2005. For at least the reasons given above, Applicants respectfully submit that the pending claims are definite and novel. Accordingly, Applicants submit that the claims in the present application are in condition for allowance, and such action is courteously solicited.

If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney at (404) 815-6500 is respectfully solicited.

No additional fees are believed due; however the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account number 11-0855.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Jamie L. Greene". The signature is fluid and cursive, with a large initial "J" and "G".

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